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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/004,562	12/05/2001	Tony Fleming	1440.1088-005	8389

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EXAMINER	
BASI, NIRMAL SINGH	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 01/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/004,562	FLEMING ET AL.	
	Examiner	Art Unit	
	Nirmal S. Basi	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,9,21-26 and 39-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,9,21-26 and 39-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/5/01, 11/10/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group I (Claims 8-9, 21-26) drawn to method of treating an allergic or inflammatory condition associated with IgE-mediated degranulation by administering an agent that binds to CD81 and inhibits IgE-mediated degranulation, on 11/10/2004, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The requirement is still deemed proper and is therefore made FINAL. Applicant has cancelled claims 12-13, 16-20, 27-38 and added new claims 39-41. Newly added claims will be examined together with Group I.

2. Amendments filed 11/10/04, 5/14/04 and 4/9/02 have been entered.

3. ***Sequence Rules Compliance***

This application fails to comply with the sequence rules, 37 CFR 1.821-1.825. Nucleotide and polypeptide sequences must be identified with the corresponding SEQ ID NO. Title 37, Code of Federal Regulations, Section 1.821 states "reference must be made to the sequence by use of the assigned identifier", the identifier being SEQ ID NO. Figure 5 contains sequences, which have not been identified by SEQ ID NO:. Their corresponding SEQ ID NO: must identify sequences in Figure 5. Correction is required.

Objections

4. The disclosure is objected to because of the following informalities:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78) as well as the relationship of instant application to the parent. Parent Application 08/954,279, is now U.S. Patent Number 6,423,501, issued July 23, 2002, and must be indicated as such.

Appropriate correction is required.

Specification

5. This application is informal in the arrangement of the specification. The specification should be arranged as follows:

(a) Title of the Invention.
(b) Cross-References to Related Applications.
etc.

The specification, page one, contains writing above the title (Attorney's Docket No., Inventors, Express mail label No. etc) which must be deleted.

6.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-9, 21-26 and 39-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is indefinite as it is not clear what is degranulated by "IgE-mediated degranulation". Further it is not clear which allergic and inflammatory conditions are associated with IgE-mediated degranulation so as to allow the metes and bounds of the claim to be determined.

Claim 23 is indefinite as it is not clear what is "contact sensitivity" so as to allow the metes and bounds of the claim to be determined.

Claims 9, 21-22, 24-26 and 39-41 are indefinite because they depend upon an indefinite base claim.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-9, 21-26 and 39-41 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method of treating passive cutaneous anaphylaxis associated with FcεRI antigen receptor and/or FcγRIII antigen receptor mediated degranulation in mast cells comprising administering to a mammal an effective amount of antibody 5D1 that binds to CD81 and inhibits FcεRI antigen receptor and/or FcγRIII antigen receptor mediated degranulation in mast cells, does not reasonably provide enablement for treatment of other allergic or inflammatory conditions or use of other agents to for treatment of other allergic or inflammatory conditions associated with IgE-mediated degranulation. The specification does not enable any person skilled in

the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims..

The scope of the claims covers the use of an undefined agent for treating a diverse list of unrelated allergic or inflammatory conditions which are inferred to be associated with IgE-mediated degranulation of an undefined structure by administering to a mammal an effective amount of an undefined agent that binds to CD81, at an undefined location, and inhibits IgE-mediated degranulation of an undefined compound. The specification discloses that antibodies (5D1) binding CD81 and inhibit FcεRI-mediated degranulation of mast cells while leaving both tyrosine phosphorylation and calcium mobilization apparently unaffected. The binding of anti-Cd81 mAb 5D1 was shown to inhibit passive cutaneous anaphylaxis in Winstar rats. The only agent shown to be effective in claimed method is anti-Cd81 mAb 5D1. The only condition that has been treated is cutaneous anaphylaxis in Winstar rats. The only IgE-mediated degranulation association has been shown with antibodies (5D1) binding to CD81 and inhibiting FcεRI-mediated degranulation of mast cells. The binding site (epitope) of the 5D1 antibody on CD81 protein is not disclosed. It is not possible to predict which other agents could bind to the CD81 and treat the diverse list of unrelated allergic or inflammatory conditions which are inferred to be associated with IgE-mediated degranulation of an undefined structure. There is no disclosure that the extensive list of claimed treatable diseases indeed are caused by a dysfunction of CD81 inhibition of FcεRI-mediated degranulation. The specification has stated that CD81 differs from other inhibitory receptors in three ways: a) unlike other

inhibitory receptors, CD81 inhibits FcεRI-mediated degranulation of mast cells while leaving both tyrosine phosphorylation and calcium mobilization apparently unaffected; b) CD81 belongs to a different structural class of proteins than other inhibitory receptors; and c) the cytoplasmic tails of CD81 lack ITIM motifs. Also disclosed is that CD81 stimulation inhibits degranulation induced through FcγRIII signaling and CD81 is a novel inhibitory receptor for FcεRI. Applicant has disclosed the assay of CD81-mediated signal transduction by measuring degranulation by a serotonin release assay through FcγRIII signaling or leukotriene assay. None of the other claimed treatable diseases, except passive cutaneous anaphylaxis, have been shown to be associated with FcεRI antigen receptor and/or FcγRIII antigen receptor mediated degranulation in mast cells by interaction with CD81.

Due to the large quantity of experimentation necessary to identify other agents/ indicators of CD81-mediated signal transduction and other "appropriate cell surface receptors" which affect CD81-mediated signal transduction, in addition to ones known in the art i.e. FcεRI and FcγRIII, the lack of guidance/direction presented in the specification regarding isolating said receptors and agents specific CD81-mediated inhibition of IgE mediated degranulation of undefined cells, the complex nature of the invention, the unpredictability of the interactions of other receptors, CD81, IgE, and its effect on signal transduction, the breadth of the claims which fail to recite what is granulated and by what agent, the diversity of diseases encompassed by the claim (diseases have no common nexus), undue experimentation would be

required of the skilled artisan to make or use the claimed invention in its full scope.

As addressed above the CD81 effect is mediated by specific Fc antigen receptors, i.e. FcϵRI and FcγRIII, which alter CD81-mediated signal transduction and can be assayed by the measurement of degranulation by serotonin release. Although the elucidation of the effects of CD81 is a continuing process the scope of the claims is governed by the disclosure and state of the art at the time of filing of the application. The scope of the claims encompasses the use of other Fc antigen receptors, any agent to treat a diverse list of diseases other than those disclosed as "enabling above". Even with a high level skill of in the art it would take undue experimentation to first discover other Fc antigen receptors which interact CD81, find agents which inhibit degranulation to practice the invention in the scope claimed. Therefore, claims 8-9, 21-26 and 39-41 are rejected under 35 U.S.C. 112, first paragraph, for the reasons given above.

Further, the deposit of anti-Cd81 mAb 5D1 is considered by the Examiner to be necessary for the enablement of the current invention because the claims require availability of the deposit. The specification does not disclose how the anti-Cd81 mAb 5D1 can be isolated without undue experimentation. The specific amino acid residues used to generate the antibody are not disclosed. It appears the antibody has not been deposited. The deposit of the anti-Cd81 mAb 5D1 in full compliance with 37 CFR §§ 1.803-1.809 is required to practice the invention the because the specification does not provide a repeatable method for

obtaining anti-Cd81 mAb 5D1 and it does not appear to be a readily available material.

Claim Rejection 35 USC § 112, 1st paragraph (Written Description)

8. Claims 8-9, 21-26 and 39-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims are drawn to method of treating an allergic or inflammatory condition associated with IgE-mediated degranulation comprising administering to a mammal an effective amount of an undisclosed agent that binds to CD81 and IgE mediated degranulation. The claims encompass agents of undefined structure. The binding site on the CD81 is not disclosed. The only agent disclosed to function in binding to CD81 and inhibiting degranulation in mast cells is an antibody, anti-CD81 mAb 5D1. Neither the hybridoma from which the antibody is not isolated, nor the antibody has been deposited. Therefore the nature of the antibody is unknown. No other agents that can function in the method as claimed are defined. The agents encompass compounds unrelated to 5D1 antibody, e.g. organic and inorganic compounds. The claims encompass use of antibodies without specific epitoipic targets on the CD81.

The common function of the "agent" used to treat the diseases, which is based upon a common property or critical technical feature of the genus claimed

is not disclosed. The claims, as written, encompass agents which vary substantially in composition. The instant disclosure of a single antibody does not adequately describe the scope of the use of the claimed genus, which encompasses a substantial variety of subgenera. A description of a genus of agents may be achieved by means of a recitation of a representative number of compounds, defined by a specific structure, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural and functional features of the claimed genus of agents. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. For example, what regions binds to CD81 and contains a definitive structural feature required for protein function? There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the agents encompassed by the claims. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of one antibody by name only is insufficient to describe the genus.

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe, enable and use the genus as broadly claimed. The skilled artisan cannot envision the detailed chemical structure of the encompassed agents and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. It is acknowledged that the skill of the artisan in the molecular biology art is high. However, in the current instance **the critical special technical feature of the agent or how the critical special technical feature encompassed by the genus claimed relates to function is not disclosed**

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid or polypeptide is itself is required. See *Fibers v. Revel*, 25 USPQ d. 1601 at 1606 (CAFC 1993) and *Amen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Therefore methods of treatment of using an agent of undefined structure is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa can be reached on 571-272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Pak

MICHAEL PAK
PRIMARY EXAMINER

NSB

Nirmal s. Basi
Art Unit 1646
January 24, 2005